Hypercoagulable State Practice Guidelines

Washington State Clinical Laboratory Advisory Council
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FOR EDUCATIONAL PURPOSES ONLY

The individual clinician is in the best position to determine which tests are most appropriate for a particular patient

Definition: Hypercoagulable state: balance of the coagulation system is tipped toward thrombosis, due to either acquired or inherited increase in pro-coagulant elements (e.g. cancer pro coagulant) or decrease in anti-coagulant elements (e.g. Protein C deficiency).

Hypercoaguable states are suspected in patients who have:

1)" Spontaneous" thrombosis without obvious associated
2) Thrombosis. Even with a concomitant risk factor, at an early age (e.g. less than 40)
3) Recurrent thrombosis, especially in different sites
4) Strong family history of thrombosis, MI or stroke in young relatives
5) Thrombosis in unusual locations (visceral thrombosis, arterial thrombosis in young person)

Acquired Disorders and applicable laboratory test

Initial testing for all patients: PT, PTT, TT, Platelet, Fibrinogen
(Refer to Coagulation Guideline for Unexplained Bleeding Disorders on the reverse side)

1) Antiphospholipid antibody (aPL) Syndrome (Lupus anticoagulant)
   Test: Anticardiolipin antibodies (ACA titers)
   Russell venom time (dRVVT) or platelet neutralization

2) Hyperhomocysteinemia (vitamin deficiency)
   Test: Serum Homocysteine

3) Dysfibrinogenemia (liver disease)
   Test: Fibrinogen, Thrombin Time, Reptilase Clotting Time

4) Heparin-induced thrombocytopenia
   Test: Heparin Antibody

5) Cancer
   Test: Use what is general practice for CA diagnosis

Inherited Disorders and applicable laboratory test

Initial testing for all patients: PT, PTT, TT, Platelet, Fibrinogen
(Refer to Coagulation Guideline for Unexplained Bleeding Disorders on the reverse side)

1) Factor V Leiden/aPC resistance (most common)
   Test: aPC (activated Protein C) resistance assay - general screen; most common reason for resistance (95%) is factor V Leiden (genetic defect in factor V) **OR** DNA analysis for factor V Leiden - determines if patient is heterozygote or homozygote

2) Factor II (Prothrombin G20210) A Deficiency
   Test: Factor II DNA Analysis

3) Protein C Deficiency, Protein S Deficiency, Antithrombin III Deficiency
   Test together with: Protein C activity, Protein S total and free antigen assays, Antithrombin activity assay

4) Hyperhomocysteinemia (metabolic defect)
   Test: Homocysteine

5) Dysfibrinogenemia/Fibrinolytic defects
   Test: Fibrinogen, Thrombin, Reptilase Clotting Time

Notes:

<u>At time of acute thrombosis:</u>

1) Protein C, Protein S, antithrombin may be falsely low due to consumption in clotting process
2) May get reactive (not causative) antiphospholipid antibodies
3) Some believe homocysteine is a acute-phase reactant

<u>When on heparin/ coumadin:</u>

1) Antithrombin is decreased to 40-60% (hep) (used as cofactor for heparin) and 10-20% (Coumadin)
2) Protein C and S may be falsely elevated by 10-20%(hep); 10-20% decreased (Coumadin)
3) Functional tests for antiphospholipid antibody may be affected by either.

References:

1. Thrombosis with a Possible Hypercoagulable State, K.Hassell MD UCHSC, Denver Co. 2001
2. Algorithm for Laboratory Investigation of Hypercoagulable State , RLA Overland Park, KS
3. CAP Consensus Conference XXXVI, Diagnosis Issues in Thrombophilia, Nov. 2001

(Coagulation Guideline for Unexplained Bleeding Disorders on reverse side)

Coagulation Guidelines For Unexplained Bleeding Disorders

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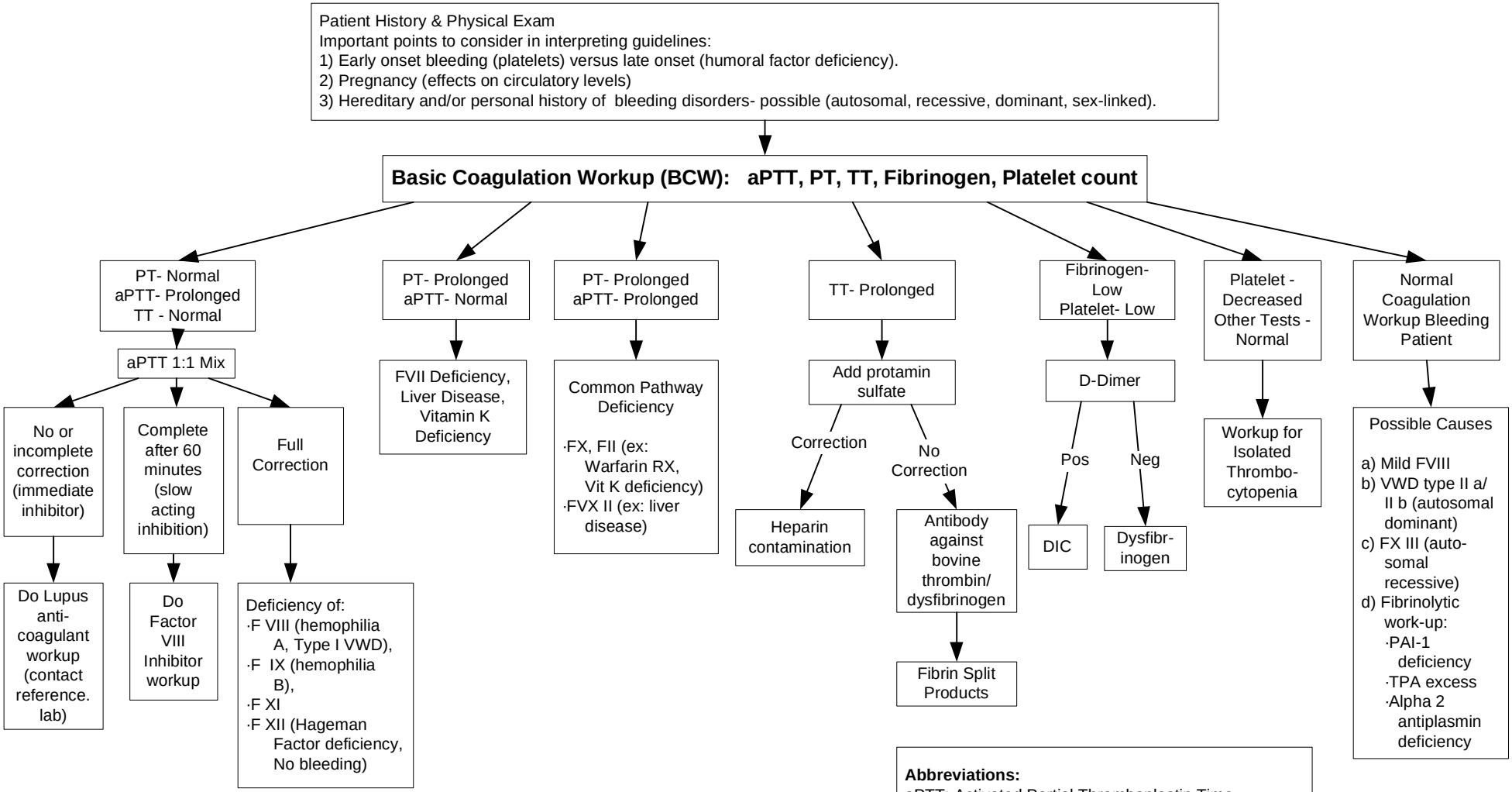

NOTE: Bleeding time maybe useful as an additional diagnostic tool for familial or acquired platelet disorders such as Von Hildebrand's disease or Ticlipod medication. In general, it is not a predictor of bleeding for surgical procedures.

REFERENCES: Work up extracted from literature and modified by University of Washington Department of Laboratory Medicine.

Abbreviations:
aPTT: Activated Partial Thromboplastin Time
DIC: Dessiminated Intravascular Coagulation
F: Factor
PAI: Plasminogen Activator Inhibitor
PT: Prothrombin Time
TPA: Tissue Plasminogen Activator
VWD: Von Willebrand's Disease